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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,860	09/05/2006	Ariel G. Notcovich	227396U	3336

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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

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11/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,860	NOTCOVICH ET AL.	
	Examiner	Art Unit	
	ANN Y. LAM	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 07 July 2008.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 29-37,39 and 41-46 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 29-37,39 and 41-46 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 29, 30, 33, 36, 37, 41, 42 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malmqvist et al., 6,200,814, in view of Newgard et al., 6,110,707, and further in view of Lambert, 20060210984, and Karlsson et al., 20050014179.

Malmqvist et al. teach controlling fluid flow over a sensing surface within a flow cell to position the fluid flow over one or more dsicrete sensing areas within the flow cell (col. 3, lines 14-18.) The term "sensitize" is referred to any process or activation of the sensing area that results in the sensing area being capable of specifically interacting with a desired analyte. The resulting surface is referred to as a “sensitized" area (col. 13, lines 31-35.) For example, the sensing area of the flow cell may be sensitized area of the flow cell cell may be sensitized by immobilization of an analyte-specific ligand (such as antigen, antibody, enzyme, DNA etc. (col. 13, lines 39-58.) Malmqvist et al. disclose that reagents used for sensitizing the sensing area (i.e., immobilization of an analyte-specific ligand) by directing flow through different inlets (some parallel, some orthogonal to each other) provided in the flow cell and that different regions can be

sensitized with same or different ligands (col. 14, line 20 – col. 15, line 7; and col. 15, line 37 -.col. 16, line 27; see also figures 13A-13E.) A gradient of amount of ligands may be provided (col. 14, lines 26-37.) Malmqvist et al. disclose laminar flow techniques to direct the fluid flow but that other techniques may be employed (col. 18, lines 42-47.) Malmqvist et al. disclose that the apparatus can be used to study how multiple biomolecular complexes are formed and how they function, and measuring interactions for the formation of complexes can be by techniques such as SPR (surface plasmon resonance) detection, or fluorescence detection (col. 16, lines 50-59.) Malmqvist et al. disclose use of flows cells for kinetic measurements in general (col. 2, lines 24-31) and it is understood that kinetic measurements are also applicable to the Malmqvist et al. flow cell (see for example col. 8, lines 38-42.)

Thus, as to claims 29, 33, 37, 38, 40, Malmqvist et al. teach, as is also claimed by Applicant, the steps of adsorbing a first binding member at microspots (the different sensitized regions), presenting a second binding member (the binding partner to the immobilized ligand), with a plurality of concentration of both binding members among the plurality of spots (i.e., the gradient of ligands), obtaining data indicative of a binding reaction between he first and second binding members at the spots (i.e., the detection methods such as SPR and fluorescence detection), and it is understood that the method involves kinetic measurements as discussed above. It is noted that the sensitizing step (i.e., step of immobilizing the first ligand binding member) is performed by introducing a flow of the ligand through the flow cell as discussed above. Because the channel of the flow cell must have been formed at some point, and the channels are used to introduce

the first binding member for adsorption, there is inherently a step of forming a first channel around a region containing the microspot. While Applicant's specification discloses a flow cell that is mountable on a surface, such limitations are not read into the claims as they are given their broadest reasonable interpretation. Thus, Malmqvist et al.'s activation step (i.e., sensitizing step) meets the limitations of Applicant's step (d) (A) (i) and (ii). It is understood that in the Malmqvist et al. disclosure, excess activating solution (first ligand binding solution) is removed which thus renders the flow cell suitable for subsequent assays.

However, Malmqvist et al. do not teach deactiving the microspot.

Newgard et al. however disclose that in coating a plate with either antigen or antibody, one will generally incubate the wells of the plate with a solution of the antigen or antibody, either overnight or for a specified period of hours. The wells of the plate will then be washed to remove incompletely adsorbed material. Any remaining available surfaces of the wells are then "coated" with a nonspecific protein that is antigenically neutral with regard to the test antisera. These include bovine serum albumin (BSA), casein and solutions of milk powder. The coating of nonspecific adsorption sites on the immobilizing surface reduces the background caused by nonspecific binding of antisera to the surface (col. 72, lines 4-14.)

Given the teachings of Newgard et al. regarding coating a surface with nonspecific protein to reduce background caused by nonspecific binding, the skilled artisan would utilize the same method taught by Newgard et al., while in regards to wells of a plate, to the invention of Malmqvist et al. to similarly improve the Malmqvist

et al. invention to reduce background noise in order to obtain more accurate assay results. Such coating of nonspecific adsoprtion sites is equivalent to Applicant's deactivating step.

Applicant claims *simultaneously* absorbing the first binding member at the discrete spots and also *simultaneously* presenting the second binding member to the first binding member at the discrete spots. Malmqvist et al. disclose that the ligand immobilization may be accomplished by directing fluid containing the ligand over the sensing surface (col. 8, lines 41-47.) A sample flow containing an analyte may then be directed into the flow cell as represented by arrow 1430, such that the sample flow contacts sensing areas 1440, 1450 and 1460. (col. 18, lines 50-53). Since Applicant does not disclose the immobilization of the ligand and analyte such that they are different from that of simply flowing fluid to contact the discrete spots, the disclosure of Malmqvist et al. in flowing the binding members as described above meet the claimed limitations.

Applicant also claims simultaneously obtaining data of binding between the first binding member and the second binding member, and simultaneously obtaining reference data from a plurality of interspots located at a surface between at least two or more microspots.

This is disclosed by Lambert in disclosing a microassay chip functionalized with at least one analyte reaction spot, and at least one, and preferably at least two homologous calibration reaction spots arranged in a line (column) perpendicular to the flow of reagent across the surface of the chip, with said at least one analyte reaction

spot being arranged in a line (row) with at least one of the calibration reaction spots such that the analyte reaction spot and the calibration reaction spot are parallel with the flow of reagent across the surface of the chip. In a more preferred embodiment, the microassay chip will include a plurality of calibration reaction spots arranged in a series of at least one and preferably at least two or more columns, each column comprised of a homologous population of calibration reaction spots, each calibration reaction spot comprised of preferably peptide nucleic acids, and each of said columns being comprised of spots of a different population of nucleic acid molecules, preferably peptide nucleic acids. See paragraph 0029. The invention is useful in proteomics for simultaneous analysis of thousands of biomolecular interactions on the surface of the microchip inserted in a flow cell cartridge and provides for normalizing or calibrating for variations in a signal intensity of binding reactions due to variations in reagent flow rate over the surface of the chip that occur as a result of the contact between the flow stream and the surfaces of the flow cell cartridge (paragraph 0002). Various techniques may be used to detect the binding interaction, including surface plasmon resonance (SPR), (paragraph 004 and 0032.)

It would have been obvious to one of ordinary skills in the art at the time the invention was made to modify the invention of Malmqvist et al. to provide calibration spots in a line between lines of analyte reaction spots because it provides for the advantage of normalizing or calibrating for variations in a signal intensity of binding reactions as disclosed by Lambert. Providing such a pattern with alternating multiple lines of analyte reaction spots and calibration spots meets the claimed limitation of a

plurality of interspots located at a surface between at least two or more microspots. Simultaneous analysis is also disclosed by Lambert (paragraph 002). The skilled artisan would have had reasonable expectation of success because both Malmqvist et al. and Lambert disclose patterns of reaction spots in a flow cell and use of surface plasmon resonance as one of the types of detection techniques that can be used.

Applicant also claims that the plurality of bindings carried out do not necessitate a regeneration step. It is disclosed in Applicant's specification in paragraph 0006 that as is known in the art and in commercially available devices, a standard kinetic binding interaction measurement includes washing and regeneration of the probe. That is, in standard kinetic binding interaction measurements, the second binding member (target) is removed so that another concentration of the target is contacted with the probe. Malmqvist et al., Newgard et al. and Lambert do not disclose a kinetic binding assay that does not necessitate a regeneration step.

However, Karlsson et al. disclose a method of determining kinetic parameters for a reversible molecular interaction between a ligand immobilized to a solid support surface and a binding partner to the ligand in solution, which comprises sequentially, without intermediate regeneration or renewal of the immobilized ligand, flowing a plurality of fluid volumes containing different known concentrations of the binding partner over the solid support surface, monitoring the momentary amount of binding partner bound to the solid support surface related to time and solution concentration of binding partner and collecting the binding data, and determining the kinetic parameters by globally fitting a predetermined kinetic model for the interaction between the binding

partner and the immobilized ligand to the collected binding data, which model allows for mass transport limitation at the solid support surface. An analytical system for carrying out the method, a computer program, a computer program product and a computer system for performing the method are also disclosed. See abstract. Karlsson et al. disclose that in the known methods that utilize regeneration, problems may arise when the ligands are covalently immobilized to the sensor surface and suitable regeneration conditions are difficult to find. Renewed binding of the ligand via an immobilized capture agent before the contacting with each new analyte concentration could then be an alternative, but has the disadvantage of consuming large amounts of ligand for the determination. See paragraph 0007. Thus, the method disclosed by Karlsson et al., which obviates the need for a regeneration step, thus avoids these problems.

It is also noted that Karlsson et al. disclosed typical chemical sensors and biosensors as well as detection methods, such as surface plasmon resonance (SPR) in paragraph 0053, presumably for performing the disclosed method. Paragraph 0054 refer to commercially available biosensors which are based on surface plasmon resonsance (SPR) and permit monitoring of surface of binding interactions in real time between a bound ligand and an analyte of interest.

It would have been obvious to one of ordinary skills in the art at the time the invention was made to utilize the teachings of Karlsson et al. to perform the kinetic binding assay using the Malmqvist et al. device (as modified by Newgard et al. and Lambert), because the method, which avoids a regeneration step, provides the

advantage of performing kinetic binding assays without the problems associated with regeneration. The skilled artisan would have had reasonable expectation of success since Karlsson et al. disclose that the method can be used with a variety of detection methods, such as surface plasmon resonance (SPR) [such as that disclosed by Malmqvist et al.] and that known detection devices can be used.

As to claim 30, SPR detection is disclosed by Malmqvist et al. (col. 16, lines 50-59.)

As to claim 36, obtaining reference data from a region of the surface not included in a microspot (i.e., another microspot used for control purposes) is disclosed by Malmqvist et al. (col. 14, lines 26-28.)

As to claim 41, forming a second channel perpendicular to the first channel is disclosed (see for example figure 11A, and see such perpendicular flows produced in figures 13A-13E.)

As to claims 42 and 46, a probe array is produced, as shown in figure 13E for example.

Claims 31, 35 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malmqvist et al., 6,200,814, in view of Newgard et al., 6,110,707, and Lambert, 20060210984, and Karlsson et al., 20050014179, as applied to claim 29 above, and further in view of Lennox et al., 6,478,839.

Malmqvist et al. disclose that the detection method may be SPR (surface Plasmon resonance) but does not specifically disclose the specific type of SPR method claimed, namely that the data indicative of a binding reaction is specifically SPR resonance angle. Lennox et al. disclose this type of SPR technique and also claims it in claim 7, reciting that regarding the SPR detection, the detector includes means for exciting surface plasmons at a plasmon resonance angle that is dependent on the optical properties of the metal film and attached monolayer, and a detector for detecting the shift in plasmon resonance angle produced by binding of ligand-binding agent to said ligand. Because Malmqvist et al. only disclose in general the use of SPR detection for detection of binding, the skilled artisan would look to the art, such as the Lennox et al. patent, for specific types of SPR that would allow for binding detection.

Claims 32, 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malmqvist et al., 6,200,814, in view of Newgard et al., 6,110,707, and Lambert, 20060210984, and Karlsson et al., 20050014179, as applied to claim 29 above, and further in view of Natesan et al., 20020048792.

Malmqvist et al. teach that the flow cell may be used for various assay purposes but do not specifically disclose that the assay is to determine dissociation constant. Natesan et al. however teach in paragraph 0113 that a number of well-characterized assays are available for determining binding affinity, usually expressed as dissociation

constant for DNA-binding proteins and the cognate DNA sequences to which they bind. While Malmqvist et al. disclose only in general the use of the flow cell for assay purposes, the skilled artisan would look to the art, such as the Natesan et al. patent, for specific types of assays to be performed.

Claims 34 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malmqvist et al., 6,200,814, in view of Newgard et al., 6,110,707, and Lambert, 20060210984, and Karlsson et al., 20050014179, and further in view of Siddigi et al., 5,541,113.

The combination of the teachings of Malmqvist et al. and Newgard et al. have been discussed above. However, neither Malmqvist et al. nor Newgard et al. teach activating a microspot by producing an electric field over the microspot.

Siddigi et al. however disclose that it is known that an electric field induces certain chemical reactions (col. 1, lines 51-56.) While the disclosure refers to a chemical reaction that can be detected, rather than for immobilizing a probe, the skilled artisan would recognize that an electric field would induce similar reactions in certain ligands that may be of interest in order to cause a reaction for immobilization purposes, and thus use of an electric field to induce reactions in the Malmqvist et al. invention would have been obvious to the skilled artisan.

Response to Arguments

Applicant's arguments with respect to the above rejected claim have been considered but are moot in view of the new ground(s) of rejection. (Applicant's arguments relate to the newly added limitations, which are addressed by the newly cited references above.)

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANN Y. LAM whose telephone number is (571)272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/
Primary Examiner, Art Unit 1641